

NS

TCAACGTT (SEQ.ID.NO:90) (ODN4) which contains the self complementary "palindrome" AACGTT (SEQ.ID.NO:105). In further optimizing this motif, it was found that ODN containing Gs at both ends showed increased stimulation, particularly if the ODN were rendered nuclease resistant by phosphorothioate modification of the terminal internucleotide linkages. ODN 1585 (GGGGTCAACGTTGAGGGGGG (SEQ ID NO: 12)), in which the first two and last five internucleotide linkages are phosphorothioate modified caused an average 25.4 fold increase in mouse spleen cell proliferation compared to an average 3.2 fold increase in proliferation included by ODN 1638, which has the same sequence as ODN 1585 except that the 10 Gs at the two ends are replaced by 10 As. The effect of the G-rich ends is *cis*; addition of an ODN with poly G ends but no CpG motif to cells along with 1638 gave no increased proliferation. For nucleic acid molecules longer than 8 base pairs, non-palindromic motifs containing an unmethylated CpG were found to be more immunostimulatory.

✓ ✓ ✓ ✓
Please delete pages 38 and 47 and replace them with substitute sheets page 38 and 47 respectively.

IN THE CLAIMS

Please cancel claim 1.

Please amend the claims as follows:

Sub D11
C1

42. (Amended) A method for increasing the responsiveness of a cancer cell to a cancer therapy, comprising:

administering to a subject having a cancer an effective amount for increasing the responsiveness of a cancer cell to a cancer therapy of an immunostimulatory nucleic acid, comprising:

5' X₁ X₂CGX₃ X₄ 3'

wherein C is unmethylated, wherein X₁X₂ and X₃X₄ are nucleotides, and wherein the sequence is not palindromic.